



## MED12 gene

mediator complex subunit 12

### Normal Function

The *MED12* gene provides instructions for making a protein called mediator complex subunit 12. As its name suggests, this protein forms one part (subunit) of the mediator complex, which is a group of about 25 proteins that work together to regulate gene activity. The mediator complex physically links transcription factors, which are proteins that influence whether genes are turned on or off, with an enzyme called RNA polymerase II. Once transcription factors are attached, this enzyme initiates gene transcription, the process by which information stored in a gene's DNA is used to build proteins.

Researchers believe that the MED12 protein is involved in many aspects of early development, including the development of nerve cells (neurons) in the brain. The MED12 protein is part of several chemical signaling pathways within cells. These pathways help direct a broad range of cellular activities, such as cell growth, cell movement (migration), and the process by which cells mature to carry out specific functions (differentiation).

### Health Conditions Related to Genetic Changes

#### FG syndrome

At least two mutations in the *MED12* gene have been found to cause FG syndrome, which is characterized by intellectual disability, behavioral problems, and physical abnormalities including weak muscle tone (hypotonia) and obstruction of the anal opening (imperforate anus).

The mutations that cause FG syndrome each change a single protein building block (amino acid) in the MED12 protein. One mutation replaces the amino acid arginine with the amino acid tryptophan at protein position 961 (written as Arg961Trp or R961W). The other replaces the amino acid glycine with the amino acid glutamic acid at protein position 958 (written as Gly958Glu or G958E). These mutations alter the structure of the MED12 protein, which likely disrupts its ability to regulate gene activity during development. However, it is unclear how the genetic changes lead to intellectual disability and the other features of FG syndrome.

#### Lujan syndrome

At least one mutation in the *MED12* gene causes Lujan syndrome, a disorder characterized by intellectual disability, behavioral problems, and physical features

including tall stature and a long, narrow face. This mutation is different than the genetic changes associated with FG syndrome (described above); the Lujan syndrome mutation replaces the amino acid asparagine with the amino acid serine at position 1007 of the MED12 protein (written as Asn1007Ser or N1007S). The mutation alters the structure of the MED12 protein and likely disrupts its ability to regulate gene activity, but it is not known how these changes affect development and lead to the specific features of Lujan syndrome.

#### Ohdo syndrome, Maat-Kievit-Brunner type

At least three *MED12* gene mutations have been found to cause the Maat-Kievit-Brunner type of Ohdo syndrome, which is a rare condition characterized by intellectual disability and distinctive facial features. The mutations that cause this disorder change single amino acids in the *MED12* gene, although they are not the same genetic changes that cause FG syndrome or Lujan syndrome (described above). The mutations that result in the Maat-Kievit-Brunner type of Ohdo syndrome change the structure of the *MED12* gene, impairing its ability to control gene activity. It is unclear how these changes lead to the particular cognitive and physical features of the disorder.

#### prostate cancer

##### tumors

Some gene mutations are acquired during a person's lifetime and are present only in certain cells. These changes, which are known as somatic mutations, are not inherited. Somatic mutations in the *MED12* gene have been found in several types of tumors, both noncancerous and cancerous.

Somatic *MED12* gene mutations are present in most uterine leiomyomas, which are noncancerous growths also known as uterine fibroids. Uterine leiomyomas are common in adult women. These growths can cause pelvic pain and abnormal bleeding, and, in some cases, lead to an inability to have biological children (infertility). Somatic *MED12* gene mutations have also been identified in some cancerous uterine tumors, including leiomyosarcomas and smooth muscle tumors of uncertain malignant potential (STUMP), and in some prostate and colorectal cancers.

Studies suggest that somatic *MED12* gene mutations alter the function of the MED12 protein, which likely disrupts normal cell signaling and impairs regulation of cell growth and other cell functions. As a result, certain cells may become able to divide in an uncontrolled way, leading to the growth of a tumor.

#### other disorders

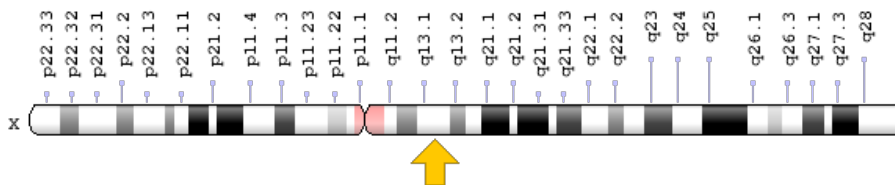
A particular variation (polymorphism) in the *MED12* gene, known as the HOPA(12bp) polymorphism, has been associated with a modestly increased risk of schizophrenia in people of northern European ancestry. This variation is an insertion of 12 extra

DNA building blocks (base pairs) in the *MED12* gene, which leads to an extra four amino acids in the MED12 protein. Because this protein is involved in several different signaling pathways, it has been difficult to determine the effects of the variation on brain function. The HOPA(12bp) polymorphism is among many factors under study to help explain the causes of schizophrenia. A large number of genetic and lifestyle factors, most of which remain unknown, likely determine the risk of developing this condition.

### Chromosomal Location

Cytogenetic Location: Xq13.1, which is the long (q) arm of the X chromosome at position 13.1

Molecular Location: base pairs 71,118,556 to 71,142,454 on the X chromosome (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

### Other Names for This Gene

- CAGH45
- HOPA
- KIAA0192
- MED12\_HUMAN
- mediator of RNA polymerase II transcription, subunit 12 homolog
- OKS
- OPA-containing protein
- OPA1
- thyroid hormone receptor-associated protein, 230 kDa subunit
- TNRC11
- TRAP230

## **Additional Information & Resources**

### Educational Resources

- Molecular Cell Biology (fourth edition, 2000): A Pol II Holoenzyme Multiprotein Complex Functions in Vivo  
<https://www.ncbi.nlm.nih.gov/books/NBK21610/#A2619>
- The Cell: A Molecular Approach (second edition, 2000): Eukaryotic RNA Polymerases and General Transcription Factors  
<https://www.ncbi.nlm.nih.gov/books/NBK9935/>

### GeneReviews

- MED12-Related Disorders  
<https://www.ncbi.nlm.nih.gov/books/NBK1676>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MED12%5BTIAB%5D%29+OR+%28mediator+complex+AND+subunit+12%5BTIAB%5D%29%29+OR+%28%28HOPA%5BTIAB%5D%29+OR+%28TRAP230%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

### OMIM

- MEDIATOR COMPLEX SUBUNIT 12  
<http://omim.org/entry/300188>

### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_MED12.html](http://atlasgeneticsoncology.org/Genes/GC_MED12.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=MED12%5Bgene%5D>
- HGNC Gene Family: Mediator complex  
<http://www.genenames.org/cgi-bin/genefamilies/set/1061>
- HGNC Gene Family: Trinucleotide repeat containing  
<http://www.genenames.org/cgi-bin/genefamilies/set/775>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=11957](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=11957)

- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/9968>
- UniProt  
<http://www.uniprot.org/uniprot/Q93074>

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